

WHAT IS CLAIMED IS:

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1. A vascular prosthesis comprising:  
an expansible structure which is implantable within a body lumen; and  
means on or within the structure for releasing mizoribine into the body lumen  
to inhibit smooth muscle cell proliferation.
2. A prosthesis as in claim 1, wherein mizoribine is released at a rate  
between 5  $\mu\text{g/day}$  to 200  $\mu\text{g/day}$ .
3. A prosthesis as in claim 1, wherein mizoribine is released at a rate  
between 10  $\mu\text{g/day}$  to 60  $\mu\text{g/day}$ .
4. A prosthesis as in claim 1, wherein mizoribine is released at an initial  
phase wherein a rate of mizoribine release is between 0  $\mu\text{g/day}$  to 50  $\mu\text{g/day}$  and a subsequent  
phase wherein a rate of mizoribine release is between 5  $\mu\text{g/day}$  to 200  $\mu\text{g/day}$ .
5. A prosthesis as in claim 1, wherein mizoribine is released at an initial  
phase wherein a rate of mizoribine release is between 5  $\mu\text{g/day}$  to 30  $\mu\text{g/day}$  and a subsequent  
phase wherein a rate of mizoribine release is between 10  $\mu\text{g/day}$  to 100  $\mu\text{g/day}$ .
6. A prosthesis as in claim 1, wherein mizoribine is released at an initial  
phase wherein a rate of mizoribine release is between 40  $\mu\text{g/day}$  to 300  $\mu\text{g/day}$  and a  
subsequent phase wherein a rate of mizoribine release is between 1  $\mu\text{g/day}$  to 100  $\mu\text{g/day}$ .
7. A prosthesis as in claim 1, wherein mizoribine is released at an initial  
phase wherein a rate of mizoribine release is between 40  $\mu\text{g/day}$  to 200  $\mu\text{g/day}$  and a  
subsequent phase wherein a rate of mizoribine release is between 10  $\mu\text{g/day}$  to 40  $\mu\text{g/day}$ .
8. A prosthesis as in claim 1, wherein mizoribine is released at a constant  
rate between 5  $\mu\text{g/day}$  to 200  $\mu\text{g/day}$ .
9. A prosthesis as in claim 1, wherein a total amount of mizoribine  
release is in a range from 100  $\mu\text{g}$  to 10 mg.
10. A prosthesis as in claim 1, wherein a total amount of mizoribine  
release is in a range from 300  $\mu\text{g}$  to 2 mg.

- 1 11. A prosthesis as in claim 1, wherein a total amount of mizoribine  
2 release is in a range from 500  $\mu\text{g}$  to 1.5 mg.
- 1 12. A prosthesis as in claim 1, wherein a mammalian tissue concentration  
2 of mizoribine at an initial phase is within a range from 0  $\mu\text{g}/\text{mg}$  of tissue to 100  $\mu\text{g}/\text{mg}$  of  
3 tissue.
- 1 13. A prosthesis as in claim 1, wherein a mammalian tissue concentration  
2 of mizoribine at an initial phase is within a range from 0  $\mu\text{g}/\text{mg}$  of tissue to 10  $\mu\text{g}/\text{mg}$  of  
3 tissue.
- 1 14. A prosthesis as in claim 1, wherein a mammalian tissue concentration  
2 of mizoribine at a subsequent phase is within a range from 1 picogram/mg of tissue to 100  
3  $\mu\text{g}/\text{mg}$  of tissue.
- 1 15. A prosthesis as in claim 1, wherein a mammalian tissue concentration  
2 of mizoribine at a subsequent phase is within a range from 1 nanogram/mg of tissue to 10  
3  $\mu\text{g}/\text{mg}$  of tissue.
- 1 16. A prosthesis as in claim 1, wherein the expansible structure is a stent or  
2 graft.
- 1 17. A prosthesis as in claim 1, wherein the means for releasing mizoribine  
2 comprises a matrix formed over at least a portion of the structure.
- 1 18. A prosthesis as in claim 17, wherein the matrix is composed of a  
2 material which undergoes degradation.
- 1 19. A prosthesis as in claim 17, wherein the matrix is composed of a  
2 nondegradable material.
- 1 20. A prosthesis as in claim 19, wherein mizoribine is released by  
2 diffusion through the nondegradable matrix.
- 1 21. A prosthesis as in claim 17, wherein the matrix comprises multiple  
2 layers, wherein at least one layer contains mizoribine and another layer contains mizoribine,  
3 at least one substance other than mizoribine, or no substance.

1           22.     A prosthesis as in claim 21, wherein the at least one substance other  
2 than mizoribine is an immunosuppressive substance selected from the group consisting of  
3 rapamycin, mycophenolic acid, riboflavin, tiazofurin, methylprednisolone, FK 506, zafurin,  
4 and methotrexate.

1           23.     A prosthesis as in claim 21, wherein the at least one substance other  
2 than mizoribine is an agent selected from the group consisting of anti-platelet agent, anti-  
3 thrombotic agent, and IIb/IIIa agent.

1           24.     A prosthesis as in claim 1, wherein the means for releasing mizoribine  
2 comprises a rate limiting barrier formed over at least a portion of the structure.

1           25.     A prosthesis as in claim 24, wherein mizoribine is released by  
2 diffusion through the rate limiting barrier.

1           26.     A prosthesis as in claim 1, wherein the means for releasing mizoribine  
2 comprises a reservoir on or within the structure containing mizoribine and a cover over the  
3 reservoir.

1           27.     A prosthesis as in claim 1, wherein mizoribine is on or within the  
2 expansible structure.

1           28.     A prosthesis as in claim 1, wherein mizoribine is disposed within a  
2 matrix or rate limiting membrane.

1           29.     A vascular prosthesis comprising:  
2 an expansible structure which is implantable within a body lumen; and  
3 a rate limiting barrier on the structure for releasing mizoribine into the body  
4 lumen to inhibit smooth muscle cell proliferation;  
5 wherein the barrier comprises multiple layers, each layer comprising parylast  
6 or paralene and having a thickness in a range from 50 nm to 10 microns.

1           30.     A prosthesis as in claim 29, wherein mizoribine is released at a rate  
2 between 5 µg/day to 200 µg/day.

1           31.     A prosthesis as in claim 29, wherein mizoribine is released at a rate  
2 between 10 µg/day to 60 µg/day.

1 32. A prosthesis as in claim 29, wherein at least one layer contains  
2 mizoribine and another layer contains mizoribine, at least one substance other than  
3 mizoribine, or no substance.

1 33. A vascular prosthesis comprising:  
2 an expansible structure;  
3 a source of mizoribine on or within the structure, wherein the mizoribine is  
4 released from the source when the expansible structure is implanted in a blood vessel; and  
5 a source of at least one other substance in addition to mizoribine on or within  
6 the structure, wherein the at least one additional substance is released from the source when  
7 the expansible structure is implanted in a blood vessel.

1 34. A prosthesis as in claim 33, wherein the at least one additional  
2 substance is an immunosuppressive substance selected from the group consisting of  
3 rapamycin, mycophenolic acid, riboflavin, tiazofurin, methylprednisolone, FK 506, zafurin,  
4 and methotrexate.

1 35. A prosthesis as in claim 33, wherein the at least one additional  
2 substance comprises at least one agent selected from the group consisting of anti-platelet  
3 agent, anti-thrombotic agent, and IIb/IIIa agent.

1 36. A prosthesis as in claim 33, wherein each source comprises a matrix,  
2 rate limiting membrane, or reservoir.

1 37. A method for inhibiting restenosis in a blood vessel following  
2 recanalization of the blood vessel, said method comprising:  
3 implanting a vascular prosthesis in the blood vessel; and  
4 releasing mizoribine into the blood vessel so as to inhibit smooth muscle cell  
5 proliferation.

Sub 5417 38. A method as in claim 37, wherein mizoribine is released at a rate  
2 between 5 µg/day to 200 µg/day.

1 39. A method as in claim 37, wherein mizoribine is released at a rate  
2 between 10 µg/day to 60 µg/day.

1 40. A method as in claim 37, wherein mizoribine is released within a time  
2 period of 1 day to 45 days in a vascular environment.

1 41. A method as in claim 37, wherein mizoribine is released within a time  
2 period of 7 days to 21 days in a vascular environment.

1 42. A method as in claim 37, further comprising releasing at least one  
2 other substance in addition to mizoribine simultaneously with mizoribine release.

1 43. A method as in claim 37, further comprising releasing at least one  
2 other substance in addition to mizoribine sequentially with mizoribine release.

1 44. A method as in claim 42 or 43, wherein the at least one additional  
2 substance is an immunosuppressive substance selected from the group consisting of  
3 rapamycin, mycophenolic acid, riboflavin, tiazofurin, methylprednisolone, FK 506, zafurin,  
4 and methotrexate.

1 45. A method as in claim 37, wherein the releasing comprises delaying  
2 substantial release of mizoribine for at least one hour following implantation of the  
3 prosthesis.

1 46. A method as in claim 45, wherein delaying release comprises slowing  
2 release from a reservoir with a material that at least partially degrades in a vascular  
3 environment over said one hour.

1 47. A method as in claim 45, wherein delaying release comprises slowing  
2 release with a matrix that at least partially degrades in a vascular environment over said one  
3 hour.

1 48. A method as in claim 45, wherein delaying release comprises slowing  
2 release with a nondegradable matrix that allows diffusion of mizoribine through the  
3 nondegradable matrix after said one hour.

1 49. A method as in claim 45, wherein delaying release comprises slowing  
2 release with a rate limiting barrier that allows diffusion of mizoribine through the barrier after  
3 said one hour.

1 50. A method as in any one of claims 47-49, wherein the prosthesis is  
2 coated with the matrix or barrier by spraying, dipping, deposition, or painting.

1 51. A method as in claim 37, wherein the prosthesis incorporates  
2 mizoribine by coating, spraying, dipping, deposition, chemical bonding, or painting  
3 mizoribine on the prosthesis.

1 *Sub B 7* 52. A method for inhibiting restenosis in a blood vessel following  
2 recanalization of the blood vessel, said method comprising:  
3 implanting a vascular prosthesis in the blood vessel; and  
4 releasing mizoribine and at least one other substance in addition to mizoribine  
5 from the prosthesis when implanted in the blood vessel.

1 53. A method as in claim 52, wherein the at least one additional substance  
2 is an immunosuppressive substance selected from the group consisting of rapamycin,  
3 mycophenolic acid, riboflavin, tiazofurin, methylprednisolone, FK 506, zafurin, and  
4 methotrexate.

1 54. A method as in claim 53, wherein the immunosuppressive substance is  
2 mycophenolic acid.

1 55. A method as in claim 53, wherein the immunosuppressive substance is  
2 methylprednisolone.

1 56. A method as in claim 55, wherein mizoribine is released within a time  
2 period of 1 day to 45 days and methylprednisolone is released within a time period of 2 days  
3 to 3 months.

1 57. A method as in claim 52, wherein the at least one additional substance  
2 comprises at least one agent selected from the group consisting of anti-platelet agent, anti-  
3 thrombotic agent, and IIb/IIIa agent.

1 58. A method as in claim 52, wherein mizoribine and the at least one  
2 additional substance are released simultaneously.

1 59. A method as in claim 52, wherein mizoribine and the at least one  
2 additional substance are released sequentially.

*Add a27*  
*Add B 37*